Thyroid Palpation Versus High-Resolution Thyroid Ultrasonography in the Detection of Nodules

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Detection of thyroid nodules by physical examination and high-resolution ultrasonography was compared using small groups of blinded, experienced physician examiners working with a sample of 2441 persons from Estonia, most of whom were Chernobyl nuclear reactor clean-up workers. A random subsample of 113 (5%) persons was subjected to triple control examinations with both physical examination and high-resolution ultrasonography. Positive high-resolution ultrasonographic findings were considerably more reproducible among different observers than were positive physical examination findings. Agreement between methods was poor. Nodules were found in 169 (6.9%) subjects by physical examination and in 249 (10.2%) subjects by high-resolution ultrasonography. Physical examination found only 53 (21%) of the 249 nodules found by high-resolution ultrasonography. High-resolution ultrasonography did not confirm the existence of 115 (68%) of the 169 nodules found by physical examination. Only 6.4% of nodules less than 0.5 cm in diameter, as based on high-resolution ultrasonographic results, were detected by physical examination. Physical examination detection improved with increasing nodule size but was still only 48.2% for nodules larger than 2 cm. Physical examination was relatively effective in detecting nodules in the isthmus of the thyroid gland but much less so for nodules in the upper pole of the gland. Clinical evaluation and epidemiologic studies of nodular thyroid disease stand to benefit from the greater sensitivity and specificity of ultrasonographic examinations. KEY WORDS: Thyroid, nodules; Nodules, thyroid; High-resolution ultrasonography; Physical examination; Palpation.

ABBREVIATIONS

HRUS, High-resolution ultrasonography; FNA, Fine needle aspiration; IOM, Institute of Medicine

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Thyroid nodules are a common clinical problem. In an autopsy study, roughly 50% of clinically normal thyroid glands had either a single or multiple thyroid nodules.[1] Ultrasonographic studies show many of these nodules to be small, with unknown clinical significance.[2] The clinical physician must first detect nodules and then identify which are probably malignant. As many as 20% of scintigraphically "cold" nodules may be malignant. Risk factors such as radiation exposure, age, family history, sex, rapid growth, pain, symptoms of compression, fixation of the nodule, and

lymphadenopathy have been used to help make clinical decisions. FNA is very helpful in diagnosing malignancy before surgery. However, the problem of nodule detection remains paramount.

The routine physical examination of the thyroid gland ordinarily includes an inspection and palpation. A more detailed, noninvasive, relatively inexpensive examination of the thyroid gland anatomy is available through HRUS. Clinical evaluations and epidemiologic studies have relied on one or both of these techniques. A general consensus that HRUS is capable of detecting reliably smaller nodules than can be found with physical examination is balanced against the reasonable probability that small nodules are not worthy of clinical pursuit. The literature on this topic consists of studies comparing small or nonsystematically collected samples. Details about reproducibility and the circumstances under which the two methods agree or disagree are scarce.[3,4]

In the course of an epidemiologic study of thyroid cancer and nodularity among clean-up workers from the nuclear accident at Chernobyl, we examined 2441 persons independently by palpation and HRUS.[5] This earlier study found little or no evidence of an association between radiation exposure at Chernobyl and thyroid nodularity. In the present report, we present a more detailed comparison of the examination results, including reproducibility and interobserver variation for each method, agreement between methods, and how the extent of agreement varies depending on host and nodule characteristics.

MATERIALS AND METHODS

The thyroid screening study was part of a larger investigation of cancer and other health outcomes among 4843 clean-up workers from the Chernobyl nuclear disaster in Estonia.[6] In the spring of 1995, 2997 of these men were invited to come to one of four cities in Estonia (Tallinn, Kohtla-Jarve, Parnu, Tartu) to have their thyroid glands examined by experienced physicians from the United States. Of the invited workers, 1984 (66%) came. In addition, 410 noninvited clean-up workers who heard of the program also came, along with 47 members of the general public who had not gone to Chernobyl. All 2394 of the clean-up workers were male, but the 47 self-invited participants included 27 women. The latter group included one 6 year old child, but all other study subjects were over the age of 20 years (mean, 40 years; maximum, 72 years). All persons who appeared and wished to be examined were examined. Only the invited workers were included in the previous study of associations between thyroid nodularity and indicators of radiation exposure,[5] but the present methodologic study includes all 2441 individuals examined. Examinations were conducted over a 10 day period.

The examining team included eight physicians with between 5 and 33 years of postgraduate experience and board certifications as listed in Table 1. Examiners 2 and 3 alternated between conducting examinations by palpation and ultrasonography, but they never performed both types of procedures on the same patient. All four of the physicians who performed physical examinations were board-certified in internal medicine; two of them were also board-certified in nuclear medicine and radiology. The other two were board-certified or board-eligible in endocrinology. All six physicians who conducted the ultrasonographic examinations were board-certified in radiology. Members of this relatively well-trained group all examine the thyroid gland routinely as part of their medical practices.

After providing written informed consent (Estonian, Russian, and English versions available) each subject underwent physical examination (inspection plus palpation) by a physician experienced in thyroid evaluations and then was examined by HRUS by a physician ultrasonologist using a Hitachi Medical Systems model EUB-405 machine (Hitachi Medical Systems America, Twinsburg, OH) equipped with a 7.5 MHz linear transducer. For the physical examination, the subjects were seated in a comfortable chair so that the examining physician could inspect the neck from the front and both sides, palpate from behind the subject with the tips of the index fingers, and instruct the subject to swallow as necessary. Each examination took approximately 1 to 2 min to complete. The following findings were recorded: size of thyroid gland (normal or enlarged), presence of palpable nodules, diameter and location of the two largest nodules, and whether the nodule in question was movable or fixed, hard or soft, and tender or nontender. Some evaluations were declared to be uncertain or indeterminate if a large neck made physical examination difficult. For the ultrasonographic examination, the subject was placed supine on a low bed with his or her shoulders supported over a pillow and the neck fully extended and exposed. Ample gel was applied to the subject's neck to ensure good performance of the transducer. The examining ultrasonologist sat to the patient's right and used the transducer in his right dominant hand. Each study took between 2 and 5 min to complete. The following ultrasonographic characteristics

Table 1: Qualifications (Board Certifications and Years of Experience) of Physicians Performing the Palpation and Ultrasonographic Examinations

Examiner	Years of Experience*	Board Certifications			
		Internal Medicine	Nuclear Medicine	Endocrinology	Radiology
Palpation					
1	5	x		†	
2‡	33	x	x		x
3‡	23	x	x		x
4	10	x		x	
Ultrasonography					
2‡	33	x	x		x
3‡	23	x	x		x
5	17	x	x		x
6	17		x		x
7	19		x		x
8	7				x

*Years of postgraduate (MD) experience.
†Board eligible in Endocrinology at time of examination.
‡Examiners 2 and 3 performed physical and ultrasound examinations (but not both types on the same patient).

were recorded: the maximum length, width, and depth of each lobe of the thyroid gland and the presence, location, size, and echo characteristics of up to two nodules. The volume of each lobe was estimated as $[(3.1416/6) \times (\text{length} \times \text{width} \times \text{depth})]$, and volumes for the lobes were summed to give a total volume. Images were recorded with a thermal paper printer for those glands that contained nodules.

The two examining physicians were blinded to each other's findings until both the physical examination and the HRUS examination were completed and the data had been recorded. After all data were recorded for each patient, a reviewing physician compared the results of the two examinations and made a decision about the advisability of an FNA biopsy for cytologic evaluation of nodules that were at least 1 cm in diameter, as determined by ultrasonography. Separate informed consent was obtained for the examination and biopsy components of the study.

In addition to the standard examination sequence, a random sample of nearly 5% of study subjects was examined independently by three palpating physicians and three ultrasonologists, as a check on interobserver variation and on the reproducibility of results for each method. All six physicians were blinded to each other's findings until all results were recorded for each examination. A decision then was made about the advisability of FNA biopsy.

Persons judged to be in need of further medical care, including treatment and ongoing surveillance, were referred to the Estonian medical care system. An Estonian physician was present at all times to help facilitate this process. If a nodule was judged to be present on the basis of the sonographic findings, a copy of the sonogram was given to the subject, and he or she was advised to give this to his or her physician. Subjects were paid a small amount in compensation for transportation costs or time lost from work.

The study protocol was reviewed and approved by institutional review boards at the National Cancer Institute in the United States and the Institute of Experimental and Clinical Medicine in Estonia.

GMBO, a program for binary logistic regression,[7] was used to test for differences and trends in the prevalence of thyroid nodules. Significance tests were performed at the $P = 0.05$ level and were two-sided except as otherwise noted. The extent of agreement between sonographic and palpation findings was quantified using the kappa statistic.[8]

RESULTS

The prevalence of thyroid nodules was found to increase with age for both methods of examination, but the trend was better defined for nodules detected by ultrasonography (Table 2). HRUS identified more nodules than physical examination, and the absolute and relative differences between methods increased with age. Among men 50 years or older, the prevalence of thyroid nodules was 15.0% based on the sonographic examinations but only 8.3% based on palpation. The sample size was small for women,

Table 2: Estimated nodule prevalence (%) by sex, age at examination, and method of examination

	Male Subjects Prevalence of Nodules (%)			Female Subjects Prevalence of Nodules (%)		
Age at Examination (yr)*	N	Ultrasound†	Palpation‡,§	N	Ultrasound||	Palpation¶
< 20	0	—	—	1	0.0	0.0
20–29	101	5.0	5.9	0	—	—
30–39	1089	8.6	5.6	5	20.0	0.0
40–49	1033	11.1	8.1	9	22.2	11.1
≥ 50	193	15.0	8.3	10	30.0	10.0
Total	2416	10.1	6.9	25	24.0	8.0

The study subjects consisted of 2394 men who were Chernobyl nuclear accident clean-up workers, plus 22 men and 25 women and girls, members of the general population who came to an examination center and asked to be examined. The total number examined (N) is shown for each age and sex group.
*Age was taken as the (unrounded) number of year of life completed.
†$P(1)$ (trend) < 0.001.
‡Percentages include 49 men for whom palpation findings were indeterminate. Exclusion of these men would increase nodule prevalences slightly.
§$P(1)$ (trend) = 0.02.
|| $P(1)$ (trend) = 0.47.
¶$P(1)$ (trend) = 0.38.

and associations with age were not well defined. The prevalence of thyroid nodules, as determined by ultrasonography, was 10% among men (mean age, 40 years), nearly 34% among women (mean age, 46 years), and 10.2 % overall.

Two hundred and forty-nine persons (10.2%) had one or more nodules detected by ultrasonography, as compared to 169 persons (6.9%) for palpation (Tables 3 to 5). Agreement between the two methods was poor. Findings were discordant for 304 (12.5%) persons. Only 53 (21.3% of the 249) persons judged to have a thyroid nodule on the basis of sonographic examinations also were judged to have a nodule on the basis of palpation. On the other hand, of 2187 persons with negative sonographic findings, 115 (5.3%) were positive for nodules by palpation. The kappa statistic, a measure of interobserver agreement, was only 0.18, which falls within the range considered to represent slight agreement.[9]

Agreement also was poor with respect to the number of nodules present. Of 152 persons in whom physical examination detected a single nodule, HRUS detected a single nodule in 36 (23.4%), multiple nodules in 10 (6.6%), and zero nodules in 106 (69.7%). Among 16 subjects judged to have two or more nodules by physical examination, five (31.25%) had multiple additional nodules by HRUS, but HRUS did not reveal any nodules for nine others (56.25%). The mean estimated thyroid gland volume (by HRUS) was significantly higher ($P < 0.001$) for glands that were judged to be diffusely enlarged on physical examination (19.5 ± 8.5 cm^3) than for those rated as being of normal size (15.3 ± 5.9 cm^3), but glands classified as multinodular by physical exami-

Table 3: Examination Results by Method of Examination

	Nodule Status by Ultrasonography				
	Absent	Solitary Nodule	Multiple Nodules	Unknown	*Total*
Nodule Status by Palpation					
Absent	2032	161	28	2	2223
Solitary Nodule	106	36	10	1	153
Multiple Nodules	9	2	5	0	16
Unknown	40	6	1	2	49*
Total	2187	205	44	5†	2441

*Examination results were indeterminate for all 49 persons (e.g., no refusals).
†Includes one refusal and four persons with an indeterminate examination.

Table 4: HRUS Findings by Examiner (Total Sample): Number (%) of Subjects

	Examiner Number											
	2		3		5		6		7		8	
Examination Result												
Negative	134	(90.5)	286	(87.5)	691	(89.4)	157	(90.8)	308	(91.7)	611	(89.3)
Positive	13	(8.8)	41	(12.5)	82	(10.6)	15	(8.7)	28	(8.3)	70	(10.2)
Indeterminate	1	(0.7)	0	(0.0)	0	(0.0)	1	(0.6)	0	(0.0)	3	(0.4)
Total	148	(100.0)	327	(100.0)	773	(100.0)	173	(100.0)	336	(100.0)	684	(100.0)

nation had approximately the same average volume (15.8 ± 6.2 cm^3) as those of normal size. Excluding the 6 year old child, thyroid volume did not show association with age at examination.

Results of the HRUS examination were more reproducible among observers than results of the physical examinations. Of 113 men randomly selected to undergo three sonographic examinations by three different physicians, 110 completed all three examinations. (Two others completed two examinations, and the other departed after just one examination.) For 93 persons, all three ultrasonographic examinations were negative for the presence of a nodule. Results for the two men examined just twice also were concordant and negative. For 13 men, all three examiners detected a nodule. Results were discordant for four persons. Thus, of 17 men found to have a nodule by any of three HRUS examiners, 13 (76.5%) were independently judged to have a nodule by all three examiners. A second nodule was detected by all three examiners for four of these men, by two examiners for two others, and by one examiner for one study subject.

Physical examination findings were less consistent, particularly with respect to positive findings. Based on the same randomly selected sample as for the HRUS examinations, physical examination findings were negative in all three examinations for 97 men, and in both examinations for three men who were examined twice. A nodule was detected by one or more physicians in 12 men. However, all three examiners detected a nodule in just one of the 12 (8.3%). This nodule was located in the isthmus of the thyroid gland and had a mean diameter (based on HRUS) of 1.8 cm. For 10 men judged to have a nodule by all three HRUS examiners, the nodules were missed in all three physical examinations. The mean size of nodules among these men was 0.8 cm (maximum, 1.6 cm).

Results for the four physicians who performed the physical examination are shown in Table 5. These data are based on the entire sample of 2441 persons. The estimated nodule prevalence ranged from 4.8% to 8.2% if the indeterminate examinations were counted as negative, and from 5.0% to 8.2% if they were excluded. Among the same workers, the prevalence of nodules as determined by HRUS varied over a much narrower range, from 9.9% to 10.4%, which suggests that the differences in physical examination findings were attributable more to interobserver variation than to differences in nodule prevalence among the study subjects. Examiners 2 and 3 were more likely to report an uncertain finding. Interestingly, these were the most experienced members of the team.

Table 5: Examination Results for Four Physicians Who Performed Clinical Examinations: Number (%) of Persons

	Number of Examiner Performing Palpation									
	1		2		3		4		*Total*	
Examination Results*										
Negative	723	(93.1)	570	(88.4)	226	(90.0)	704	(91.7)	2223	(91.1)
Positive	47	(6.0)	47	(7.3)	12	(4.8)	63	(8.2)	169	(6.9)
Indeterminate	7	(0.9)	28	(4.3)	13	(5.2)	1	(0.1)	49	(2.0)
Total	777	(100.0)	645	(100.0)	251	(100.0)	768	(100.0)	2441	(100.0)

*The prevalence of nodules based on ultrasonographic examinations for the same patients was 10.4% for examiner 1, 9.9% for examiner 2, 10.0% for examiner 3, and 10.3% for examiner 4.

If HRUS is considered to be a more sensitive and specific method than palpation for the detection of thyroid nodules, as these and other data would suggest, it can be used as a standard against which the performance of palpation can be evaluated. Among men judged to have one or more nodules in the sonographic examinations, whether a nodule also was detected by palpation was strongly related to nodule size (Table 6). Only 6.4% of nodules less than 0.5 cm in diameter were detected by palpation. Although the proportion increased with size, only 40% of nodules over 1.5 cm and 48% of those over 2.0 cm were ascertained. This indicates that more than half of nodules greater than 2 cm were missed. Among nodules detected by ultrasonography, 57% were in the right lobe, 39% were in the left lobe, and 10% were in the isthmus. Palpation was considerably less effective for nodules in the right or left lobes than for those in the isthmus, and it was very ineffective for nodules in the upper pole of the gland. The prevalence of nodules detected by palpation was not significantly associated with nodule type (solid, cystic, mixed) or estimated thyroid volume (Table 6).

FNA biopsy was performed on 94 persons. Biopsy results revealed two papillary carcinomas (2.3 and 2.8 cm in diameter) and three follicular tumors (1.5 to 2.0 cm). After surgery, the follicular tumors were found to be adenomas. One of the two cancer patients and one of the three adenoma patients were identified as having a thyroid nodule by physical examination. Ultrasonograms of two tumors missed by physical examination are shown in Figures 1 and 2. (It also should be noted that the follicular tumor that was palpable was missed by ultrasonography.)

DISCUSSION

Strengths of the present comparative study include its large size, inclusion of persons who were not selected for examination because of suspicion of thyroid disease, independent examinations by highly

Table 6: Ultrasonographic Results by Nodule Characteristics and Thyroid Gland Characteristics*

	Characteristic Number†	Number (%) with Nodule by Palpation		*P*‡
Maximum nodule diameter (cm)				*< 0.001*
< 0.50	31	2	(6.4)	
0.50–0.99	107	21	(19.6)	
1.00–1.49	61	10	(16.4)	
1.50–1.99	23	7	(30.4)	
≥ 2.00	27	13	(48.2)	
Location of nodule in thyroid gland:				
Lobe of gland (laterality):				< 0.001
Right lobe	142	29	(20.4)	
Left lobe	97	16	(16.5)	
Isthmus	10	8	(80.0)	
Pole of gland (cephalad-caudad)§:				0.01
Upper pole	41	2	(4.9)	
Middle pole	99	22	(22.2)	
Lower pole	99	21	(21.2)	
Nodule type:				0.25
Solid	92	24	(26.1)	
Cystic	17	2	(11.8)	
Mixed (solid and cystic)	140	27	(19.3)	
Volume of thyroid gland (cm^3)¶:				0.66
0–14.1	59	11	(18.6)	
14.2–18.7	65	16	(24.6)	
18.8–25.3	62	15	(24.2)	
25.4–67	62	11	(17.7)	
Unknown	1	0	(0.0)	

*Result for the 249 persons with a nodule detected by ultrasonography who also were judged to have a nodule by physical examination (palpation).
†Number of persons undergoing palpation among those with a nodule detected by ultrasonography.
‡Test for trend in proportion for nodule size and thyroid gland volume; test for homogeneity for nodule location and type.
§Pole not coded for nodules located in isthmus.
¶Calculated as a function of length, width, and depth. Lobe volume = [3.1416 / 6 × (length × width × depth)]. Volumes for the two lobes were then summed.

trained and experienced clinical and sonographic examiners who were blinded to the level of radiation exposure (at Chernobyl), and the inclusion of a substudy of interobserver variation for each method.

Our literature review found only a limited number of studies that employed relatively small numbers of subjects for direct comparison of HRUS and physical examination. Furthermore, these studies were not always blinded, and some used consensus results for physical examination data. The results of examinations done in this fashion may be typical of clinical practice but easily bias the nonblinded ultrasonographic observer. A concern about consensus physical examination of the thyroid gland remains. Could the senior physician performing the physical examination have a dominant opinion that swayed the other physician's opinion? This could be thought of as an "alpha male" effect, which could bias a study's result. Clinical physicians in the daily practice of medicine accept this as part of the consultative process, but its effect on the statistical quality of an epidemiologic study is difficult to assess when reading the reports that rely on consensus physical examination of the thyroid gland. The data reported in this paper are free of these difficulties.

Clinical Implications

Results confirm previous assessments that physical examination alone is an insensitive and relatively nonreproducible method for detecting thyroid nodules, and further the findings indicate that the underestimation is not limited to small, clinically insignificant nodules. Even nodules measuring more than 2 cm on sonograms were missed half of the time in physical examinations by experienced clinicians who routinely perform thyroid evaluations. These failures to detect large nodules occurred despite the physical examiners' collective impression that the study subjects were not particularly hard to examine. Most had relatively slender necks, and all but a handful were fully cooperative. Without the true gold standard of thyroid gland resection and pathologic examination, it is not possible to calculate the actual sensitivities and specificities of either method of examination. However, assuming that sonographically invisible nodules are relatively uncommon, ultrasonographic findings provide a basis for approximate estimates of sensitivity and specificity of palpation. On the basis of these data we would estimate the sensitivity to be about 21% and the specificity to be about 95%. The sensitivity was approximately 27% for nodules 1 cm or less in diameter and 40% for those over 1.5 cm. Results also indicate that physical examination (1) works reasonably well for the detection of nodules in the isthmus of the thyroid but not for the far more common nodules lying deeper within the glands and (2) is an unreliable method for distinguishing solitary and multiple nodules. These patterns generally agree with the findings of previous smaller clinical and epidemiologic studies.[3,4,10,11]

The authors in one such study noted that "the overall agreement between the two methods is poor."[3] Possible reasons for such poor agreement include difficulties in palpating nodules smaller than 1 cm, the dependence of palpation examinations on thyroid gland firmness and lobulation, location of nodules within the thyroid gland, and the amount of overlying soft tissue. Ultrasonography is affected to a lesser extent by these factors and can reveal even small nodules deep within the gland.

Neither physical examination nor HRUS can distinguish reliably between benign and malignant

Figure 1 Longitudinal HRUS image of a papillary carcinoma of the right lobe of the thyroid gland with a mean diameter of about 2 cm. It was not palpable.

Figure 2 Longitudinal HRUS image of a large follicular adenoma, greater than 2 cm in diameter, replacing most of the left lobe of the thyroid gland. It was not palpable.

thyroid nodules. Physical examination characteristics of a hard nodule, irregular shape, irregular surface, and fixation to adjacent structures suggest malignancy of the papillary carcinoma variety. Solitary palpable nodules have been regarded as more suggestive of malignancy than multiple nodules, although this view has been disputed.[12] In either case, physical examination does not accurately differentiate between single and multiple nodules.

HRUS findings of irregular shape in a hypoechoic lesion with unclear borders and tiny calcifications also suggest papillary carcinoma. An excellent specificity for malignancy has been claimed for both physical examination and HRUS (98% and 90%, respectively). A somewhat lower sensitivity for physical examination and HRUS for malignancy was reported (63% and 78%, respectively).[13] By HRUS, a simple majority of malignancies may be hypoechoic; poorly defined nodule margins may correspond to malignant invasion; and thin, complete "halos" around nodules suggest benign lesions, although this last observation has not been uniformly supported.[14–16] The finding of microcalcifications in nodules has been reported to have a 93% specificity for malignancy but only a 36% sensitivity.[16] Small, nonpalpable lesions do not warrant further evaluation unless HRUS findings suggest malignancy.[17] The diagnosis of malignancy remains the province of cytologic (FNA biopsy) and histologic examination.[14–18] In our series of 2441 persons (mean age, 40 years) not referred for examination because of suspected thyroid disease, ultrasonography identified 249 people with one or more nodule, 94 received FNA biopsy, and we identified two thyroid cancers and three follicular adenomas, all of which were resected.

Current recommendations for the clinical use of HRUS limit it to the detection of nodules in patients with a high risk for thyroid cancer, presurgical planning to map the extent of thyroid cancer, and guidance for FNA biopsy.[19] The use of ultrasonography has not been recommended for the detection of thyroid nodules in the general population, in part because of the view that small nodules are clinically unimportant and palpation is reliable for detecting large nodules.[12] However, the belief that an appropriately trained physician or other health care provider will detect lesions of 1.5 cm or greater reliably (those presumed to be clinically significant and worthy of FNA examination)[20] is not supported by results of this study. Furthermore, palpation is a relatively crude method for assessing nodule size. The use of physical examination to monitor changes in nodule size among patients with sonographically detected nodules less than 1.5 cm in diameter might not be supportable, given that one half of nodules 2 cm or less in size were missed altogether by a group of physicians using palpation whose training and experience in the area exceeds that of the average physician. For patients at especially high risk for developing a thyroid carcinoma, such as those treated with radiation therapy for Hodgkin's lymphoma, routine clinical follow-up with HRUS has been recommended.[21]

Epidemiologic Implications

Epidemiologic studies of the prevalence of thyroid neoplasms after radiation exposure have been hampered by lack of control groups, uncertainty in radiation dosimetry, and small numbers of thyroid lesions detected by the physical examination method. Estimates of excess relative risk and absolute risk of cancer tend to have relatively wide confidence intervals.[17]

Large studies exist that have depended on physical examination to establish the prevalence of thyroid nodules. Marshall Islanders who were exposed to head and neck radiation as children and Japanese atomic bomb survivors surveyed for radiation effects in the thyroid gland have been examined by both physical examination and HRUS in studies that cover almost 50 years of follow-up examinations.[22–27] Working primarily with physical examination, a series of surveys of children irradiated in infancy for enlarged thymus glands or tinea capitis and adults who had undergone multiple fluoroscopic examinations have established a lifelong increased risk of thyroid nodular disease.[28–31] In these reports the confidence intervals for risk estimates are wide. The results of physical examination and HRUS in our study suggest that a large number of nodules would have been recorded by HRUS in those populations, and risk coefficients would have been estimated more precisely. The radiation dose–response relationships in these groups would still have been strongly positive. However, it is interesting to speculate that a closer estimate of relative risks would have been possible given the availability of HRUS.

Studies relying on multiple examiner consensus physical examination of thousands of subjects exposed to fallout from the nuclear weapons test programs in the American southwest initially reported exposed and control groups with low prevalences of thyroid nodules.[32,33] Nodules were detected in about 2% for the low-dose controls and in 4% for the high-dose subjects. Statistical analysis did not show a significant dose-response relationship for

either carcinomas or benign nodules.[34] The "baby boomer" population of the United States is now being considered by the IOM for thyroid screening to find possible radiogenic thyroid nodules and cancer linked to the same Nevada nuclear weapons tests. The IOM of the National Academy of Sciences will make its recommendation to the National Institutes of Health in June of 1998 about the advisability of thyroid screening. The findings in this report have immediate, practical implications.[35]

CONCLUSIONS

If the health care provider in the usual practice setting relies on his or her fingers for nodule detection, a great number of nodules of significant size will be missed that would have been pursued clinically with FNA biopsy or surgery if they had been known to be present. Should HRUS be used for screening the general population? Should it be reserved for those patients with clinical risk factors? A long-term, outcome-based study to determine the clinical efficacy and cost-benefit ratio of HRUS in the general population would be expensive and logistically complex. Clearly, known nodules that are clinically judged to be innocent should be followed by HRUS.

The greater sensitivity and reproducibility of HRUS make it the preferred method for use in epidemiologic studies of nodular thyroid disease. HRUS improves statistical power both by identifying more outcomes and by decreasing misclassification. We would anticipate as well that ultrasonography would be a more sensitive method for detecting possible associations with other risk factors, such as exposure to low-dose ionizing radiation. Investigators must take care to ensure that research objectives do not interfere with appropriate clinical management of nodules detected by ultrasonography.

Large-scale epidemiologic studies might be streamlined by using HRUS as the first method of examination, with palpation being used thereafter only to select those persons who could appropriately be referred for FNA biopsy under palpation control. We find needle biopsy under palpation, when possible, to be a faster and less complicated technique than using ultrasonography for guiding aspiration. Those persons with nodules not clearly palpable could undergo FNA biopsy with HRUS targeting. Immediate feedback to the FNA biopsy physician by a cytopathologist performing rapid Diffquik (Baxter Pharmaceuticals, McGaw Park, IL) staining for microscopic examination of part of the specimen is critical to the success of either approach. For a study of radiation-induced thyroid cancer and nodularity in a large screening program, the use of HRUS as the principal examination tool would ensure good sensitivity, specificity, and scanning speed.

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